

REMARKS

The Specification has been amended to include reference to application number PCT/GB2003/003686, filed August 22, 2003, which in turn, claims priority from Great Britain Application Serial No. GB 0303924.5, filed February 20, 2003, which in turn claims priority from Great Britain Application Serial No. 0230037.4, filed December 23, 2002, which in turn claims priority from United States Application Serial No. 10/227,131, filed August 23, 2002.

The Claims have been amended to reduce multiple dependencies and to conform claims more closely to U.S. practice.

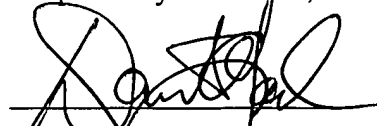
In this connection, applicant wishes to point out that the claims being treated as original claims for the purposes of this filing and this Preliminary Amendment correspond to the claims submitted to the International Bureau as of November 23, 2004 and that were acknowledged and considered in the International Preliminary Examination Report (IPER) mailed January 14, 2005. A separate copy of said claims as filed before the International Bureau is also enclosed and confirmation that said claims are pending herein is requested.

Claims 37 and 46 are amended herein to correct typographical errors. No issue of new matter is introduced via these amendments.

New claims 51-54 are presented herein. Support for new claims 51-54 is found in the original claims and throughout the Specification as filed. Support for new claims 51-54 is found, for example, in original claims 29, 34, 36 and 46, respectively. No issue of new matter is introduced by this amendment.

Entry of the foregoing amendments and favorable processing in the National Phase before the United States Patent and Trademark Office is courteously solicited.

Respectfully submitted,



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Date: February 23, 2005

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CLAIMS

1. A modified nucleotide or nucleoside molecule comprising a purine or pyrimidine base and a ribose or deoxyribose sugar moiety having a removable 3'-OH blocking group covalently attached thereto, such that the 3' carbon atom has attached a group of the structure

-O-Z

wherein Z is any of $-C(R^{IV})_2-O-R''$, $-C(R')_2-N(R'')_2$, $-C(R')_2-N(H)R''$, $-C(R^{IV})_2-S-R''$ and $-C(R')_2-F$,

wherein $-C(R^{IV})_2-O-R''$ is of the formula $-CR^4(R^5)-O-CR^4(R^5)-OR^6$ or of the formula $-CR^4(R^5)-O-CR^4(R^5)-SR^6$; and wherein $-C(R^{IV})_2-S-R''$ is of the formula $-CR^4(R^5)-S-CR^4(R^5)-OR^6$ or of the formula $-CR^4(R^5)-S-CR^4(R^5)-SR^6$;

wherein each R'' is or is part of a removable protecting group;

each R' is independently a hydrogen atom, an alkyl, substituted alkyl, arylalkyl, alkenyl, alkynyl, aryl, heteroaryl, heterocyclic, acyl, cyano, alkoxy, aryloxy, heteroaryloxy or amido group, or a detectable label attached through a linking group; or $(R')_2$ represents an alkylidene group of formula $=C(R''')_2$, wherein each R''' may be the same or different and is selected from the group comprising hydrogen and halogen atoms and alkyl groups;

each R^4 and R^5 is independently a hydrogen atom or an alkyl group;

R^6 is alkyl, cycloalkyl, alkenyl, cycloalkenyl or benzyl; and

wherein said molecule may be reacted to yield an intermediate in which each R'' is exchanged for H or, where Z is $-C(R')_2-F$, the F is exchanged for OH, SH or NH_2 , preferably OH, which intermediate dissociates under aqueous conditions to afford a molecule with a free 3'OH; with the proviso that where Z is $-C(R^{IV})_2-S-R''$, both R^{IV} groups are not H.

2. A molecule according to claim 1 wherein R' is an alkyl or substituted alkyl.

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3. A molecule according to claim 1 or claim 2
wherein -Z is of formula $-C(R')_2-N_3$.

4. A molecule according to any one of claims 1 to 3
5 wherein Z is an azidomethyl group.

5. A molecule according to claim 1 or claim 2
wherein R" is a benzyl or substituted benzyl group.

10 6. A molecule according to any preceding claim
wherein said base is linked to a detectable label via
a cleavable linker or a non-cleavable linker.

15 7. A molecule according to claim 6 wherein said
linker is cleavable.

20 8. A molecule according to any one of claims 1 to 5
wherein a detectable label is linked to the molecule
through the blocking group by a cleavable or non-
cleavable linker.

9. A molecule according to any one of claims 6 to 8
wherein said detectable label is a fluorophore.

25 10. A molecule according to any one of claims 6 to 9
wherein said linker is acid labile, photolabile or
contains a disulfide linkage.

30 11. A modified nucleotide molecule as claimed in any
one of claims 1 to 10 which comprises one or more ^{32}P
atoms in its phosphate portion.

12. A nucleoside, nucleotide or polynucleotide